Clinical Epidemiology

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Validity of the recorded codes of gonadotropin-releasing hormone agonist treatment and orchiectomies in the Danish National Patient Registry

This article was published in the following Dove Press journal:
Clinical Epidemiology
16 June 2012
Number of times this article has been viewed

Christina Gade Jespersen[1,2]
Michael Borre[1]
Mette Nørgaard[2]

[1]Department of Urology, Aarhus University Hospital, Aarhus, Denmark; [2]Department of Clinical Epidemiology, Institute of Clinical Medicine, Aarhus University Hospital, Aarhus, Denmark

Purpose: Large-scale observational studies based on existing medical databases may have an important role in studies of long-term effects of different treatments in prostate cancer patients if the coding of the treatment is valid. We therefore estimated the positive predictive value (PPV) and negative predictive value (NPV) of hospital codes for gonadotropin-releasing hormone (GnRH) agonist treatment and orchiectomies in the Danish National Patient Registry (DNPR).

Patients and methods: From Danish prostate cancer patients we selected 100 patients who were registered as users of GnRH agonists, 100 patients who were registered as nonusers of GnRH agonists, 50 patients who were registered as bilateral orchidectomized, and 50 patients who were not registered as orchidectomized in the DNPR between January 1, 2002 and December 31, 2008. From the patients' medical files we recorded codes for GnRH agonist treatment and orchiectomies, including dates of treatment from date of first prostate cancer diagnosis and onward.

Results: The PPV of GnRH agonist treatment coding in the DNPR was 93% (95% confidence interval [CI]: 86.1–97.1), and the NPV was 94% (95% CI: 87.4–97.8). Both the PPV and NPV of orchiectomy coding in the DNPR were 100% (97.5% CI: 92.9–100).

Conclusion: We measured the validity of codes for GnRH agonist treatment and orchiectomies in the DNPR among prostate cancer patients and found high PPV and NPV. Thus, the DNPR remains a valuable tool for clinical epidemiological studies of GnRH agonist treatment and orchiectomies in the treatment of prostate cancer.

Keywords: prostate cancer, orchiectomy, positive predictive value, negative predictive value

Introduction

Prostate cancer is the most common malignancy in men and the second most common cause of death from cancer in men in Western countries.[1] Treatment modalities include prostatectomy, radiation therapy, orchiectomy, and androgen deprivation therapy (ADT). The most commonly used ADT is gonadotropin-releasing hormone (GnRH) agonist treatment. The indication for ADT has previously been symptomatic locally advanced and metastatic prostate cancer, but the use of ADT has increased during the last decade with the advocacy of adjuvant ADT in otherwise asymptomatic patients with locally advanced prostate cancer, and the inclusion of neoadjuvant temporary ADT in the multimodal treatment of localized prostate cancer.[2] Adverse effects of the

Correspondence: Christina Gade Jespersen
Department of Clinical Medicine, Aarhus University Hospital, Brendstrupgaardsvej 100, 8200 Aarhus N, Denmark
Tel +45 78 45 90 30
Fax +45 86 78 55 28
Email christina.gade@ki.au.dk

hypogonadism caused by ADT, eg, loss of libido, erectile dysfunction, hot flashes, nonmetastatic bone fractures, obesity, insulin resistance, and metabolic syndrome, are well known,[3] but other adverse effects, such as coronary artery disease and stroke, are not yet fully examined and need further research.[4–7] Bilateral orchiectomy also leads to hypogonadism, and possibly similar adverse effects could thus occur in orchidectomized patients.

Medical registries are important data sources for epidemiological and clinical research. Using data from a medical registry greatly increases the efficiency and cost-effectiveness of such research. The large size of many databases offers the potential for precise estimates of effect and the possibility of studying rare exposures or outcomes. The validity of information in medical registries is crucial for using the data in research. The Danish National Patient Registry (DNPR) is an electronic medical registry, and the validity of the codes for GnRH agonist treatment and orchiectomies recorded in the DNPR has never been assessed.

In support of future studies of GnRH agonist treatment and orchiectomies, we therefore estimated the positive predictive value (PPV) and negative predictive value (NPV) of recorded codes for GnRH agonist treatment and orchiectomies among prostate cancer patients, using data from medical file reviews as the reference.

Material and methods

Denmark has 5.3 million inhabitants who are provided with free tax-supported health care by the National Health Service. A unique ten-digit civil registration number is, since 1968, assigned to all Danish residents by the Central Office of Civil Registration, and this number allows unambiguous linkage between all Danish registries.[8] We linked data from the Danish Civil Registration System, the Danish Cancer Registry, and the DNPR and identified patients diagnosed with prostate cancer in the period January 1, 2002 through December 31, 2008.

Identifying patients with prostate cancer

We identified men with prostate cancer through the Danish Cancer Registry.[9] This is a population-based, nationwide registry with data on incident cancer in Denmark since 1943. Data include civil registration number and stage at diagnosis. All diagnoses have been reclassified according to the International Classification of Diseases 10th revision (ICD-10). We used ICD-10 code DC61.9 to identify patients with prostate cancer.

The Danish National Patient Registry

This registry contains data on all somatic hospital admissions since 1977 and on outpatient and emergency room visits since 1995. It includes dates of admission and discharge, medical treatments, surgical procedures, and up to 20 diagnoses coded by physicians at discharge according to ICD-8 until 1993 and ICD-10 thereafter.[10]

Validation of DNPR information with patients' medical records

We selected 100 prostate cancer patients from two different hospitals, one referral and one district hospital, registered with the code "BWHC," which covers hormonal and antihormonal antineoplastic treatment, in the DNPR between January 1, 2002 and December 31, 2008. This code includes GnRH agonist treatment and treatment with antiandrogens. GnRH agonists are exclusively distributed by urologists at outpatient urological clinics or urological departments. The urologists are responsible for coding the treatment, and the administrative code BWHC is reported to the DNPR by secretaries. We reviewed the medical files of the patients from date of first prostate cancer diagnosis and onward to confirm whether GnRH agonist treatment was recorded, and we recorded the date of first GnRH agonist treatment according to the medical file. The information from the DNPR was compared with the information on GnRH agonist treatment in the medical files. We classified the information on GnRH treatment in DNPR as correct if a GnRH treatment could be confirmed through the medical file at the same date or any time after prostate cancer diagnosis.

We similarly selected 100 prostate cancer patients who had no registered BWHC code in the DNPR at any time. We reviewed these patients' medical files and ruled out GnRH agonist treatment if no such treatment was recorded in the medical files at any time after prostate cancer diagnosis.

Surgical codes in Denmark are coded by the operating surgeon according to the Nordic Medico-Statistical Committee's classification of surgical procedures. We selected 50 prostate cancer patients registered with one of the codes for bilateral orchiectomy, KKFC10/KKFC13/KKFC15, in the DNPR, and reviewed the medical files of the patients from date of first prostate cancer diagnosis and onward to confirm whether the patient had been orchidectomized, and we recorded date of orchiectomy according to the medical file. We classified the information on orchiectomy in the DNPR as correct if the orchiectomy could be confirmed through the medical file at the same date or any time after prostate cancer diagnosis.

Finally, we selected 50 prostate cancer patients who had no registered orchiectomy code in the DNPR at any time. We reviewed these patients' medical files and ruled out orchiectomy if no such procedure was recorded in the medical files at any time after prostate cancer diagnosis.

Statistical analyses

We used information from patients' medical files (all files were available) as gold standard. We calculated the PPV and NPV for the codes for GnRH agonist treatment/bilateral orchiectomies in the DNPR using the results from the medical file review as a reference. The PPV was the proportion of patients registered with BWHC or KKFC10/13/15 in the DNPR who also had this according to their medical file. The NPV was the proportion of patients not registered with BWHC or KKFC10/13/15 in the DNPR who also did not receive GnRH agonist treatment or who were orchidectomized according to their medical file. Furthermore, we calculated the PPV and NPV for the two periods 2002–2005 and 2006–2008. The confidence intervals (CI) of the PPV and NPV of the orchiectomies are presented with one-sided 97.5% CI. All other estimates are presented with two-sided 95% CI. We additionally computed the difference between date of first GnRH agonist treatment or date of orchiectomy in the medical file and the corresponding date in the DNPR in months. Statistical analyses were performed using STATA software (Version 11, SE; StataCorp, College Station, TX). The study was approved by the Danish Data Protection Agency (Journal No 2009-41-3793).

Results

The median age at diagnosis of the 200 prostate cancer patients with or without the GnRH agonist treatment code was 71 years (range: 48–95 years). Out of 100 patients who were registered with BWHC in the DNPR, 93 patients received GnRH agonist treatment according to their medical files, while seven patients did not receive a GnRH agonist treatment at any time; thus, the PPV was 93% (95% CI: 86.1–97.1; Table 1). For the period 2002–2005 the PPV was 92% (95% CI: 80.8–97.8), and for the period 2006–2008 it was 94% (95% CI: 83.5–98.7). Six of the seven patients not receiving GnRH agonist treatment were treated with antiandrogens according to their medical files. The remaining patient was treated with an injection of a vitamin K antagonist at the registered date of BWHC. Of the 93 patients who received GnRH agonist treatment, 66 (71%) received the treatment according to their medical file at the same date as registered in the DNPR, 21 patients (23%) received it 3 months before the registered date in the DNPR, four patients (4%) received it 6 months before the registered date in the DNPR, and the remaining two patients received it 8 and 16 months earlier, respectively (Table 2).

Table 1 Validity of the codes for gonadotropin-releasing hormone agonist treatment and orchiectomies among 300 Danish prostate cancer patients in the Danish National Patient Registry: January 1 2002–December 31 2008

DNPR	Medical files		Total
	Yes	No	
GnRH agonist			
Yes	93	7	100
No	6	94	100
PPV			93/(93 + 7) × 100 = 93% (95% CI, 86.1–97.1)
NPV			94/(94 + 6) × 100 = 94% (95% CI, 87.4–97.8)
Orchiectomy			
Yes	50	0	50
No	0	50	50
PPV			50/(50 + 0) × 100 = 100% (97.5% CI, 92.9–100)
NPV			50/(50 + 0) × 100 = 100% (97.5% CI, 92.9–100)

Abbreviations: GnRH, gonadotropin-releasing hormone; DNPR, Danish National Patient Registry; PPV, positive predictive value; NPV, negative predictive value; CI, confidence interval.

Out of 100 patients who were not registered with BWHC in the DNPR, 94 patients did not receive GnRH agonist treatment at any time according to their medical files, while six patients received GnRH agonist treatment; thus, the NPV was 94% (95% CI: 87.4–97.8; Table 1). The NPV was 94% in both 2002–2005 and 2006–2008. The median age at diagnosis of the 100 prostate cancer patients with or without an orchiectomy code was 75 years (range: 53–92 years).

Table 2 Accuracy of the recorded date of first gonadotropin-releasing hormone agonist treatment code in the Danish National Patient Registry compared with the date of first gonadotropin-releasing hormone agonist treatment in the corresponding medical file in 93 Danish prostate cancer patients between January 1 2002 and December 31 2008

GnRH date in DNPR – GnRH date in medical file, months	Number of patients, (%)
0	66 (71)
3	21 (23)
6	4 (4)
8	1 (1)
16	1 (1)

Abbreviations: GnRH, gonadotropin-releasing hormone; DNPR, Danish National Patient Registry.

All 50 patients registered with KKFC10/13/15 in the DNPR were orchidectomized according to their medical file, resulting in a PPV of 100% (97.5% CI: 92.9–100; Table 1), and all dates of orchiectomies in the DNPR were identical with the dates recorded in the medical file. None of the patients without a KKFC10/13/15 code in the DNPR were orchidectomized according to their medical file, resulting in an NPV of 100% (97.5% CI: 92.9–100; Table 1).

There was no substantial difference in any of the results from the referral and the district hospital.

Discussion

In this study we found a good agreement between codes in the DNPR for GnRH agonist treatment (PPV of 93%) and orchiectomies (100%) and the actual treatment according to the medical files, and also a good agreement for patients not treated with GnRH agonists (NPV of 94%) or orchiectomies (100%). To our knowledge, no other study has been published on the coding of GnRH agonist treatment or orchiectomies in the DNPR or any other registries.

Whether the data quality documented in our study is sufficient for registry-based studies depends on the proposed research questions and the study design used.[11] In recent observational studies of adverse effects of ADT among prostate cancer patients, the comparison cohorts consisted of prostate cancer patients who did not use ADT.[4–7] In such studies, a high NPV, as well as a high PPV, is important in order to prevent associations to be biased toward unity.

If data from the DNPR are to be used to assess changes in treatment with GnRH agonists over time, the PPV must remain sufficiently stable in order to obtain valid estimates. We examined changes of the validity of the codes over time by splitting the study period into two periods, 2002–2005 and 2006–2008, and found only a minor increase of the PPV from 92% to 94% during the study period, suggesting that data can be used to asses GnRH agonist treatment changes over time. In our study, only 6% of the codes for GnRH agonist treatment in the DNPR were more than 3 months off, according to the medical files. For most purposes this inaccuracy will have no influence on results, except for studies where the outcome is expected immediately after onset of GnRH agonist treatment.

One limitation of the study is that the code BWHC also covers treatment with antiandrogens. Antiandrogens are often used in combination with GnRH agonist treatment, whereas monotherapy with an antiandrogen is rare, ranging between 5% and 7% of all prostate cancer patients,[6,12] consistent with what we found in this study (6%). Therefore, we do not expect this minor misclassification to alter results.

The registered data in the DNPR on orchiectomies are very accurate, and because the outcome of this surgical procedure is irreversible and immediately effective, it makes data very suitable for epidemiological research.

Conclusion

In this study we found high PPV and NPV of codes for GnRH agonist treatment and orchiectomies in the DNPR among prostate cancer patients. Thus, the DNPR remains a valuable tool for clinical epidemiological studies of GnRH agonist treatment and orchiectomies in the treatment of prostate cancer.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clin*. 2010;60(5):277–300.
2. Cooperberg MR, Lubeck DP, Mehta SS, Carroll PR, CaPSURE. Time trends in clinical risk stratification for prostate cancer: Implications for outcomes (data from CaPSURE). *J Urol*. 2003;170(6 Pt 2):S21–S15; discussion S26–S27.
3. Uroweb.org. European Association of Urology: guidelines on prostate cancer, 2012. Available at: http://www.uroweb.org/gls/pdf/08%20Prostate%20Cancer_LR%20March%2013th%202012.pdf. Accessed May 14, 2012.
4. Keating NL, O'Malley AJ, Freedland SJ, Smith MR. Diabetes and cardiovascular disease during androgen deprivation therapy: observational study of veterans with prostate cancer. *J Natl Cancer Inst*. 2010;102(1):39–46.
5. Saigal CS, Gore JL, Krupski TL, et al. Androgen deprivation therapy increases cardiovascular morbidity in men with prostate cancer. *Cancer*. 2007;110(7):1493–1500.
6. Azoulay L, Yin H, Benayoun S, Renoux C, Boivin JF, Suissa S. Androgen-deprivation therapy and the risk of stroke in patients with prostate cancer. *Eur Urol*. 2011;60(6):1244–1250.
7. Alibhai SM, Duong-Hua M, Sutradhar R, et al. Impact of androgen deprivation therapy on cardiovascular disease and diabetes. *J Clin Oncol*. 2009;27(21):3452–3458.
8. Frank L. Epidemiology. When an entire country is a cohort. *Science*. 2000;287(5462):2398–2399.
9. Storm HH, Michelsen EV, Clemmensen IH, Pihl J. The danish cancer registry – history, content, quality and use. *Dan Med Bull*. 1997; 44(5):535–539.
10. Lynge E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public Health*. 2011;39(Suppl 7):30–33.
11. Sorensen HT, Sabroe S, Olsen J. A framework for evaluation of secondary data sources for epidemiological research. *Int J Epidemiol*. 1996;25(2):435–442.
12. Martin-Merino E, Johansson S, Morris T, Garcia Rodriguez LA. Androgen deprivation therapy and the risk of coronary heart disease and heart failure in patients with prostate cancer: a nested case-control study in UK primary care. *Drug Saf*. 2011;34(11): 1061–1077.